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NO EVIDENCE OF STOCHASTIC RESONANCE IN POSTURAL SWAY RESPONSE TO NOISY
GALVANIC VESTIBULAR STIMULATION IN HEALTHY YOUNG ADULTS

By

Dominique Rice

A thesis submitted in partial fulfillment
Of the requirements for the degree

Of

MASTERS OF SCIENCE

In

Kinesiology

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UTAH STATE UNIVERSITY
Logan, Utah

2021

ABSTRACT

No Evidence of Stochastic Resonance in Postural Sway Response to Noisy Galvanic

Vestibular Stimulation in Healthy Young Adults

By

Dominique Rice, Masters of Science

Utah State University, 2021

Major Professor: Dr. Christopher Dakin

Department: Kinesiology

The transcutaneous application of a sub-sensory electrical stimulation to the vestibular afferents, known as noisy galvanic vestibular stimulation (nGVS), is thought to cause a reduction in postural sway at optimal amplitude intensities due to a mechanism known as stochastic resonance (SR). SR is a phenomenon whereby the addition of low amplitude noise to a non-linear system can be beneficial rather than detrimental. In humans, behavioral markers of SR in postural sway have been inconsistent, potentially due to insufficient power or false positives. Therefore, the main purpose of this study was to determine whether the frequency of observing SR-like effects improves with recording duration and if not, whether SR-like effects can emerge as a result of chance (false positives). To test this, sixteen healthy participants stood on a force plate and on foam with eyes closed and feet together while they were provided 300-second trials of nGVS (ten times longer than what is commonly used) at six stimulation amplitudes (100 μ A, 200 μ A, 300 μ A, 500 μ A, 700 μ A and a sham of 0 μ A). To identify SR-like effects, the center of pressure (COP) area and COP path length were recorded. To quantify the

presence of SR-like behavior, COP measures were fit with an SR model and a linear model, then the fit of the two models were compared using the Akaike information criterion (AIC) and the Bayesian information criterion (BIC). Less than 25% of the data fit the SR model better than the linear model. In addition, by randomly extracting 30-second data segments from the 0 μ A sham trials, in which no SR-like behavior should be present, the SR model was found to be the best fit model up to 44% of the time in the COP area and up to 38% of the time in the COP path length data. These data support recent findings that suggest SR-like behavior may have been observed by chance in previous studies and true SR may be limited, or absent, in measures of postural sway in healthy young adults.

(47 pages)

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INTRODUCTION

A common contributor to falls in older adults and patients with vestibular processing disorders is the deterioration of the vestibular hair cells that sense motion as well as the atrophy and desensitization of vestibular afferent nerve fibers that transmit motion information to the brain (Alvarez et al., 2000; Iwasaki & Yamasoba, 2015; Merchant et al., 2000; Richter, 1980; Wuehr et al., 2017). These vestibular impairments can cause dizziness and loss of stability that can lead to life-altering falls (Herssens & McCrum, 2019; Iwasaki & Yamasoba, 2015; Wuehr et al., 2017). The consequences of these falls are costly in terms of hospitalization, health care, and nursing home fees. They also lead to a variety of repercussions such as fear of falling, onset of functional decline, decreased mobility, depression, and increased burden on family and society (Clegg et al., 2013; Florence et al., 2018; Gale et al., 2016; Grossman et al., 2018; Guinand et al., 2012; Juraschek et al., 2019; Shankar et al., 2017; Sibley et al., 2014).

Noisy Galvanic Vestibular Stimulation

The frequency and severity of the consequences of a fall warrant the pursuit of interventions that lessen the risk of falling due to vestibular impairments. Recent evidence suggests that a sensory intervention known as noisy galvanic vestibular stimulation (nGVS) may be an option for decreasing fall risk in older adults and those with impaired vestibular information processing (Fujimoto et al., 2016; Inukai, Otsuru, et al., 2018; Iwasaki et al., 2014; Wuehr, Nusser, Decker, et al., 2016; Wuehr et al., 2017). Noisy GVS is the transcutaneous application of imperceptible electrical noise to the vestibular afferents via electrodes placed over the mastoid processes behind each ear

(Fujimoto et al., 2016; Inukai, Masaki, et al., 2018; Iwasaki et al., 2014; Mulavara et al., 2011; Wuehr et al., 2017). Given that vestibular impairments can decrease the sensitivity of vestibular afferents, the ability of the vestibular system to detect natural motion becomes diminished, potentially contributing to postural instability (Iwasaki & Yamasoba, 2015; Mulavara et al., 2011). Noisy GVS is thought to artificially enhance the strength of natural motion signals by enabling sub-threshold stimuli to exceed the activation thresholds of the impaired afferents through an effect known as stochastic resonance (SR) (Figure 1) (Cheng et al., 2021; Fujimoto et al., 2016; Goel et al., 2015; Inukai, Masaki, et al., 2018; Inukai, Otsuru et al., 2018; Iwasaki et al., 2014; Moss et al., 2004; Mulavara et al., 2015; Nooristani et al., 2019; Pal et al., 2009; Wuehr, Nusser, Krafczyk, et al., 2016).

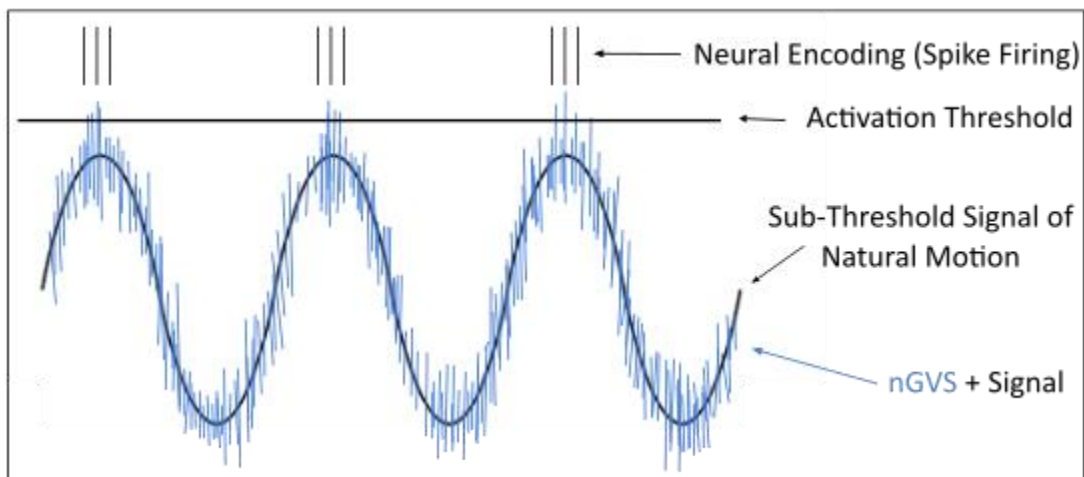
Stochastic Resonance

SR is the phenomenon whereby the addition of an external noise to a non-linear system brings about an enhanced response (Benzi et al., 1981; Collins et al., 1995; Douglass et al., 1993; McDonnell & Abbot, 2009). Typically, noise is considered to be a hinderance to signal identification and transmission, however, in some circumstances, for instance when an internal non-linear signal is too weak to be perceived, the addition of an external and optimal amount of non-zero noise can have a cooperative effect that will enhance detectability of the signal (Figure 1 and 2) (Collins et al., 2003; McDonnell & Abbot, 2009). The SR phenomenon in relation to balance control can be plotted as an inverted bell-shaped curve where postural sway measures decrease as the intensity of added noise approaches optimal amplitudes, and then increase (get worse) as the noise

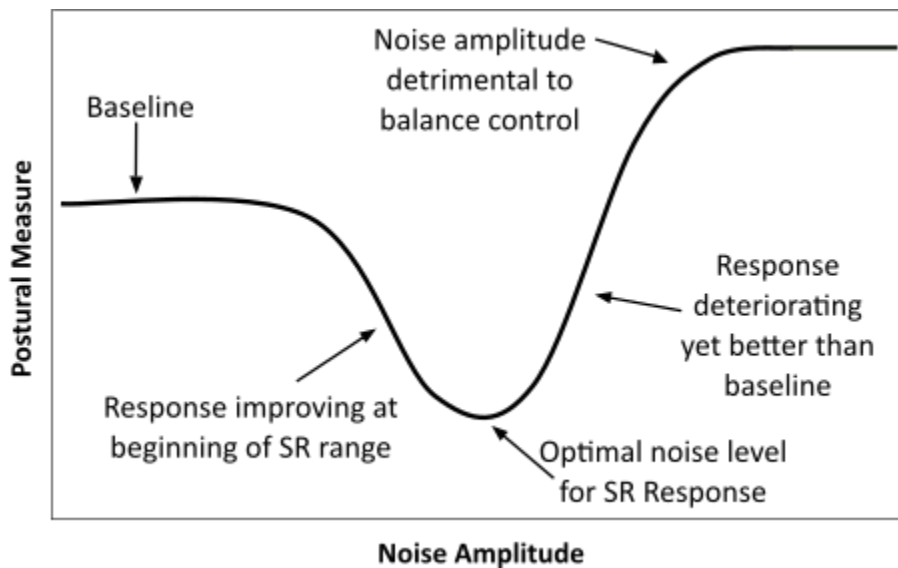
intensity increases past optimum and becomes detrimental to balance control (Figure 2) (Asslander et al., 2021; Galvan-Garza et al., 2018). Stochastic resonance has been proposed to be the underlying mechanism driving nGVS-related improvements to gait symmetry in healthy participants, and those with bilateral vestibulopathy (Iwasaki et al., 2018; Wuehr, Nusser, Decker, et al., 2016; Wuehr, Nusser, Krafczyk, et al., 2016), as well as nGVS-related decreases in postural sway observed during quiet standing in younger and older adults, and in patients with vestibular dysfunction or neurodegenerative disease (Goel et al., 2015; Inukai, Masaki, et al., 2018; Inukai, Otsuru et al., 2018; Iwasaki et al., 2014; Mulavara et al., 2011; Pal et al., 2009; Samoudi et al., 2015).

Figure 1

Effects of Stochastic Resonance



Notes. The addition of an optimal amplitude of noise (nGVS) to a sub-threshold signal enables the previously undetectable signal of natural motion to be encoded by vestibular afferents (spike firing (action potentials) in the top row) (Moss et al., 2004).

Figure 2*Pseudo Bell-Shaped SR Curve*

Note. Typical SR behavior represented in postural data resembles an inverted bell-shaped curve where postural measures decrease as the added noise approaches optimal amplitudes then the measures increase above baseline measures as the noise intensity becomes detrimental to balance control

Unfortunately, there is very little evidence within nGVS research to support the espoused theory that SR is the mechanism driving the postural response to this stimulation. One reason for this is that the focus of nGVS researcher has been on demonstrating the effect of an “optimal” nGVS intensity. Therefore, most nGVS studies involve pre-test “thresholding” to identify a *single* ideal amplitude. “Thresholding” is a procedure that is carried out prior to the experimental task to determine the optimal nGVS amplitudes for eliciting the best postural response for each individual participant (Fujimoto et al., 2016; Fujimoto et al., 2018; Goel et al., 2015; Mulavara et al., 2011; Mulavara et al., 2015; Piccolo et al., 2020; Samoudi et al., 2015; Sprenger et al., 2020; Temple et al., 2018; Woll et al., 2019; Wuehr, Nusser, Decker, et al., 2016; Wuehr,

Nusser, Krafczyk, et al., 2016). Henceforth, only one nGVS amplitude is used during nGVS experimental testing, negating the ability to plot the relationship between a range of amplitude intensities and the postural sway results that would demonstrate whether there was a decreasing trend in the measures at an intermediate range of intensities that would be indicative of SR.

Despite many reports of nGVS's effect on postural sway, both the methods and the results reported between studies have been variable and inconsistent. There is little agreement on how to determine the appropriate stimulation parameters, and little discourse on what constitutes evidence of SR in balance control. Also, nGVS studies typically observe a response to the stimulation in only a fraction of participants, and these effects are often observed using only small samples of behavior. This last point in particular is worth emphasizing: Most of the studies examining nGVS's impact on postural sway have used relatively short recording durations of 30 to 60 seconds. Sway behavior is not consistent over time, therefore derivative measures based on short recording durations are susceptible to high variability. Indeed, to fully capture the natural statistics of sway, recording durations of greater than 120 seconds are necessary for eyes-open conditions, and between 300 to 360 seconds are necessary for eyes-closed conditions (Carpenter et al., 2000; van der Kooij et al., 2011). This observation raises concern that some of these studies may have observed SR-like trends in their data that are in fact a result of random variability due to the short recording periods. Recently, Asslander et al., (2021) contributed to this uncertainty further by finding little evidence of SR-like changes to postural behavior establishing the need to more

rigorously investigate the presence of SR-like behavior in measures of human postural sway (Galvan-Garza et al., 2018; Goel et al., 2015; Iwasaki et al., 2014; Iwasaki et al., 2018; Mulavara et al., 2011; Mulavara et al., 2015).

Aims

This thesis has two aims, the first is to determine whether the behavioral changes to postural stability that occur in response to the addition of nGVS, show evidence of SR when applied systematically across a range of sub-sensory amplitude levels (100 μ A, 200 μ A, 300 μ A, 500 μ A, 700 μ A and a sham of 0 μ A). To address the first aim, five hypotheses were tested.

Hypothesis 1: To identify SR-like behaviors and overcome the limitations of short recording periods, nGVS was applied for 300-seconds, rather than the 30-60 seconds that is normally used. The presence of SR was determined by fitting an SR model (described in the methods: Galvan-Garza et al., 2018; Gammaitoni et al., 1998) and a linear model to individual participant data and then comparing the quality of fit of the two models. I hypothesized that, assuming SR is present, with longer recording times I will observe the SR model fitting the data best at a higher frequency across participants than the linear model.

Hypothesis 2: If SR was not observed in hypothesis 1, I investigated whether this is due to time-dependent effects, namely, whether the SR phenomenon is most noticeable early in exposure to nGVS stimulation but diminishes over time resulting in wash out with longer recording durations. To investigate this, individual participant data was divided into ten consecutive 30-second segments and each 30-second segment (across

stimulus amplitudes) was fit with the SR and linear models. I hypothesized that no time-dependent effects would be observed and the proportion of best-fit models (SR versus linear) would remain constant over time.

Hypothesis 3: To further investigate whether the observation of SR-like behavior in nGVS research is dependent on recording duration, the individual participant data was divided into ten different length segments (30 seconds, 60 seconds, 90 seconds....300 seconds) extracted from a random start position within the 300-second trial. These segments were fit with the SR and linear models to determine if the length of data effects how often the SR model is the best fit. I hypothesized that if SR is present, then the proportion of the SR model being the better fit would increase with time as data-segment length increases.

Hypothesis 4: A common observation in nGVS studies is that participants with vestibular impairments and/or poorer balance control at baseline tend to be affected more by nGVS than participants with normal balance at baseline (Fujimoto et al., 2019; Herssens & McCrum, 2019; Inukai, Otsuru, et al., 2018; Inukai, Masaki, et al., 2018). Since nGVS appears to have greater efficacy when balance is unstable or impaired, I compared the proportion of times the SR model is the best fit between standing on a compliant surface (foam) versus standing on a firm surface (no foam). I hypothesized that if SR is present then the SR model would fit the individual participant data more frequently than the linear model in participants standing on foam versus standing on a firm surface.

Hypothesis 5: One final way to check for an effect of SR, this time across participants, was to construct a histogram of the optimal stimulation frequency (that produced the lowest postural sway measures), exhibited by each participant. Though the optimal frequency may vary between participants, a general pattern should emerge that the most common optimal frequency falls between the sham (0 μ A) and the highest stimulation amplitude (700 μ A). I hypothesized that if SR is present, then the stimulation amplitude which most often produces the best results for the measures of sway would be at an intermediate stimulation amplitude (between 0 μ A and 700 μ A). SR would then present as an 'inverted U' shaped histogram.

The second aim of this study was to determine how frequently an SR-like pattern could arise in measures of postural sway simply by chance. To address this aim, I examined how frequently the SR model was the best fit during periods when stimulation was not being provided. To do this, I divided the sham trial (0 μ A) for each participant into 30-second segments and compared the fit of the SR model versus the linear model. I hypothesized that if SR is present then the frequency at which SR-like behavior is observed by chance in the no-stimulation trials would be less than the frequency at which SR-like behavior is observed during the stimulation trials.

METHODS

Participants

Sixteen healthy young participants were recruited through SONA, flyers, and word-of-mouth from the student body of Utah State University in Logan, Utah, USA. Participants were between the ages of 18 and 30 (age: 23.44 ± 3.12 years; height: 170.34 ± 9.48 cm;

weight: 68.12 ± 10.77 kgs; 10 females). The participants filled out pre-screening health questionnaires (Par-Q and EVS), Covid-19 protocol statements, and informed consent forms via the REDCap software. Exclusion criteria included recent lower extremity injury or chronic sensory dysfunction (neural, vestibular, or visual) as well as the inability to stand for more than 15 minutes. This protocol (#10700) was approved by the Utah State University IRB in April 2021.

Pre-test Control Measurement

Initially, participants were instructed to stand with no shoes on, their feet together on the force plate while their foot placement was marked with tape. The same procedure was repeated on a 10 cm thick piece of foam placed on the force plate. Once the foot placement was marked, the participants were instructed to stand with no shoes, eyes closed, feet together and arms by their sides in order to record a 300-second pre-test baseline control on the bare force plate. This baseline pre-test control was recorded for each participant prior to the application of the stimulation electrodes

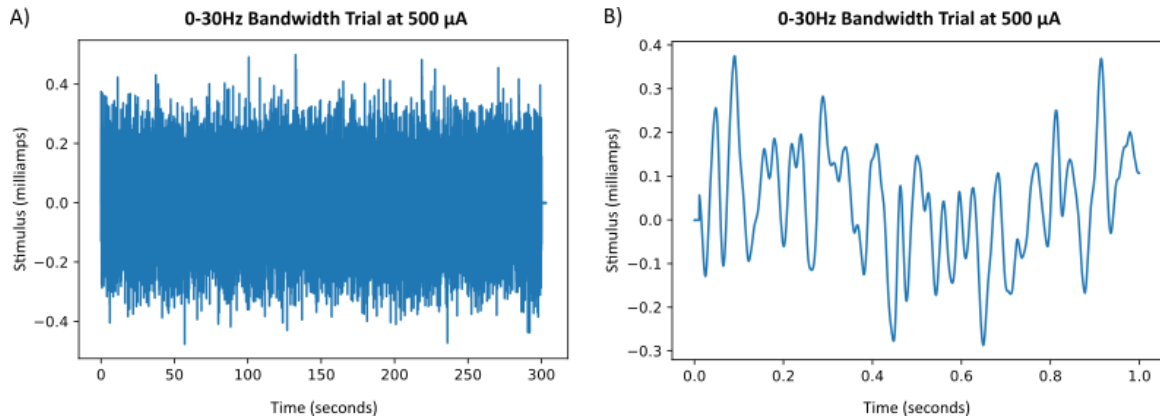
Electrode Application

After the baseline data was collected, participants were instructed to remove any earrings and tie-up long hair, then the area behind the ears was cleaned with an alcohol swab. The vestibular stimulation electrodes were covered in a half-centimeter thick layer of *Spectra 360* electrode gel and attached to the mastoid processes using medical adhesive tape. The carbon rubber electrodes ($\sim 9 \text{ cm}^2$) were applied in a bipolar binaural electrode configuration. A 0–30 Hz zero-mean, white noise electrical stimuli was generated using Labview software (National Instruments, Austin, TX, USA) and delivered

from a digital to analogue converter (PXIe-6363, National Instruments, Austin, TX, USA) to an isolated constant current stimulator (STMISOL, Biopac, Goleta, CA, USA) (Figure 3).

Figure 3

White Noise nGVS Stimulation Profile



Note. Example of the zero mean white noise nGVS stimulation profile with an amplitude of 500 μ A. Panel 'A' portrays the bandwidth limited white noise waveform of the full 300-second stimulation profile. Panel 'B' represents a one-second segment in order to better display the random nature of the waveform.

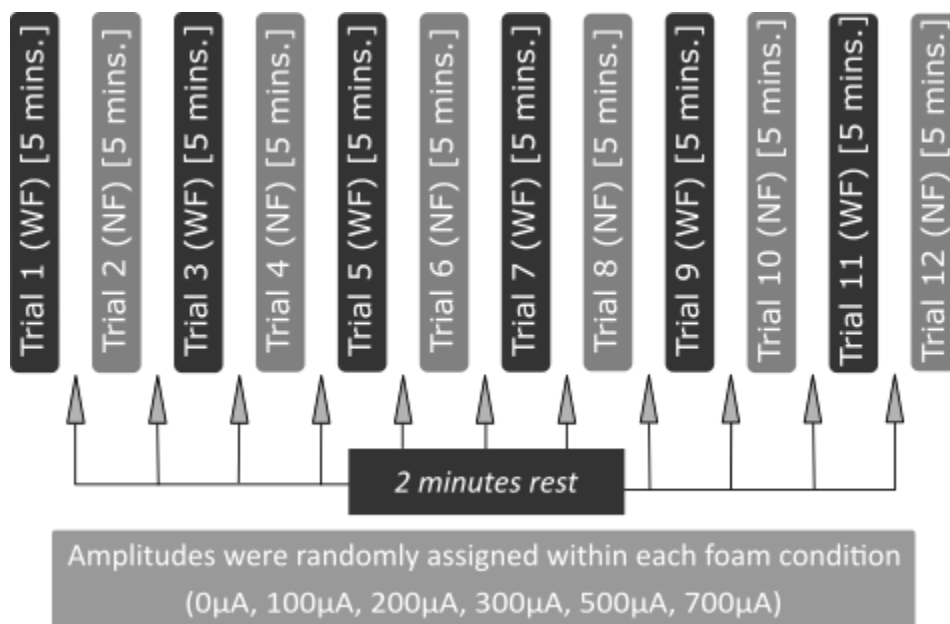
Experimental Procedure

For each stimulation trial, the participant was instructed to stand without their shoes on, feet together (in the marked location), arms by their sides, chin level with the floor, and their eyes closed. The stimulation procedure involved twelve 300-second quiet standing trials. The stimulus bandwidth was 0-30 Hz for each trial except the sham trials, during which no stimulation was provided (Galvan-Garza et al., 2018; Goel et al., 2015; Mulavara et al., 2011; Mulavara et al., 2015; Piccolo et al., 2020; Samoudi et al., 2015; Temple et al., 2018; Wuehr, Nusser, Decker, et al., 2016; Wuehr, Nusser, Krafczyk, et al., 2016). The twelve trials alternated between standing directly on the force plate

and standing on foam on the force plate. For each trial, within each condition (no foam/with foam), one of six different stimulation amplitudes were delivered via the electrodes [100 μ A, 200 μ A, 300 μ A, 500 μ A, 700 μ A and a sham of 0 μ A] (Figure 4). The order of amplitude delivery was randomized, however, the no foam/with foam conditions were alternated to reduce the fatigue associated with standing on foam for long periods of time. Between each trial, participants were instructed to sit and rest for 2-minutes (Figure 4). Participants were blind to which amplitude was being delivered.

Figure 4

Experimental Procedures



Note. nGVS pseudo-randomized stimulation procedure involved alternating foam conditions (no foam/with foam) and randomized delivery of amplitude intensities within each foam condition. A 300-second control/baseline trial (not pictured in this diagram) was recorded prior to the application of the stimulation electrodes and prior to the quiet standing experimental task.

Data Analysis

First Aim:

Hypothesis 1: In order to determine whether SR is present, I analyzed individual-participant data using a longer than customary sampling duration of 300 seconds. First, the data for each 300-second nGVS amplitude trial were processed offline using a custom Matlab script (version 1984-2021a; Mathworks, USA) in which two postural measures were calculated: COP area and COP path length. COP was calculated using the equation for COP from the Bertec force plate manual:

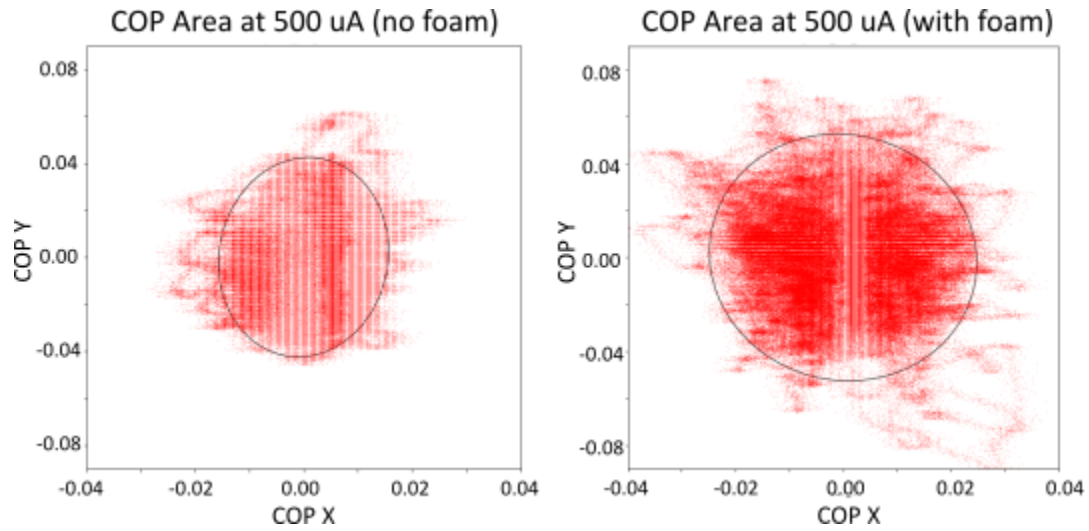
$$COP_x = (-h * F_x - M_y) / F_z$$

$$COP_y = (-h * F_y + M_x) / F_z$$

Then COP was centered by removing the mean in both anterior-posterior and mediolateral directions. From the COP data for each participant, an ellipse that captured 95% of the area of the sway path was fit to the data and the area of the ellipses were measured to provide a pseudo measure of COP 'sway' area. A total of 12 COP area ellipses were generated for each participant: 100 μ A/with foam, 100 μ A/no foam, 200 μ A/with foam, 200 μ A/no foam, 300 μ A/with foam, 300 μ A/no foam, 500 μ A/with foam, 500 μ A/no foam, 700 μ A/with foam, 700 μ A/no foam and a sham of 0 μ A/with foam, 0 μ A/no foam (For an example of an ellipse see: Figure 5). Next, the COP area data for each amplitude of stimulation delivered to each participant, in each condition (no foam/with foam), were normalized to the sham condition, to account for individual differences in baseline sway, and fit with an SR and an intercept only linear model.

Figure 5

Examples of 95% Ellipses Sway Area



Note. Examples of 95% ellipses (black) of the COP area (red) at 500 μ A from the same participant: One with foam (with foam) and one with no foam (no foam).

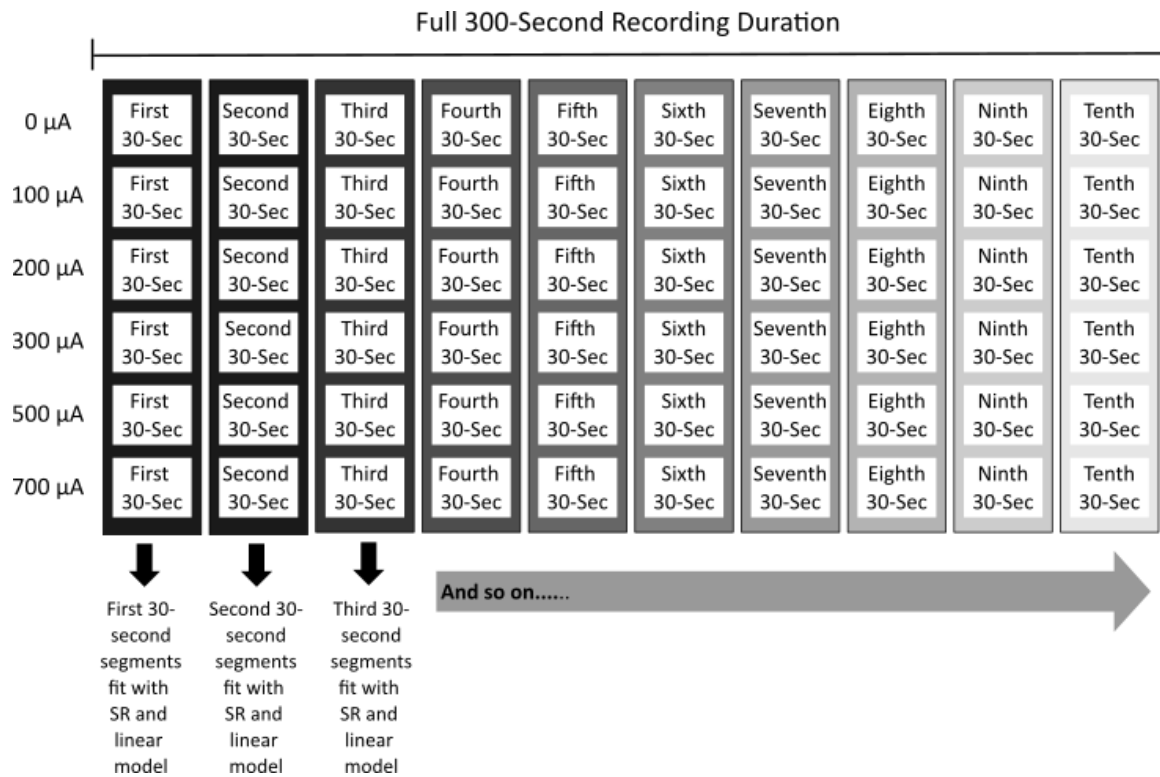
The same procedure was repeated using COP path length. The SR curve/model is defined by equation 1 (Galvan-Garza et al., 2018; Gammaitoni et al., 1998).

$$A = A_0 \frac{\lambda}{q^2} \frac{r(q^2)}{(4r(q^2) + \omega_0^2)^{1/2}} \quad (1)$$

Where, A_0 is amplitude of periodic forcing, ω_0 is frequency of periodic forcing and λ is the quartic potential parameter (depth and spread of potential well) (Galvan-Garza et al., 2018; Rouvas-Nicolis & Nicolis, 2007). In order to ensure the SR model captured a decrease in the measures (COP area or COP path length) at some intermediate stimulus amplitude, only convex SR-curves were retained. Specifically, I kept SR models that were the best fit only if the lowest COP measure was neither the first (sham 0 μ A) nor the last (700 μ A) data point (enforcing some degree of convexity). SR models that were the best

fit but that were linear, or concave, were replaced with the linear model. This SR model has been used to capture SR-like behavior across multiple stimulation amplitudes previously but is based off of a first principles model of SR behavior in which a particle of mass moves between two wells (Gammaitoni et al., 1998). Because of this, the parameters of the model are meaningful to the original double well model, but are not directly relatable and/or useful for interpretation of the data recorded here. Therefore, the only information retained and used from this model was whether it was the best fit. Finally, the linear and the SR models were compared using the Akaike information criterion (AIC) as well as the Bayesian information criterion (BIC) to determine which model better fit the data. Both AIC and BIC consider the quality of model fit as well as the number of model parameters (a model being penalized for having more parameters). When the SR model was determined to be the best fit to the individual participant data, the percentage decrease of the COP measure from baseline were calculated.

Hypothesis 2: In order to investigate whether the strength of the SR phenomenon depends on stimulus exposure time, each 300-second nGVS amplitude trial (control, 0 μ A, 100 μ A, 200 μ A, 300 μ A, 500 μ A, and 700 μ A, for both no foam and with foam) was divided into ten 30-second segments, for each participant (Figure 6). If the SR phenomenon was strongest early in the recording and declined with time, then in the first 30-second segment the proportion of participants who fit the SR model would be greater than in later time segments. Thus, each 30-second time segment across stimulus amplitudes was fit with the SR and linear model (Figure 6) and compared using the

Figure 6*30-Second Segment Analysis Procedure*

Note. Each 300-second nGVS amplitude trial was divided into 30-second segments. The first 30-second segments from each nGVS amplitude trial were fit for comparison with an SR and a linear model. Next, the second 30-second segments from each trial were fit for comparison with an SR and a linear model, and so on, until all ten 30-second segments from the full recording period were fit with the models. The proportion of SR to linear model fits, across participants, across all ten 30-second segments were then assessed with a linear model to determine whether there was a change in the proportion of SR models over time.

methods described in hypothesis 1. Then, to assess whether the early time segments were more responsive to SR than later time segments, the proportions of participants who fit the SR model across time segments were modeled as both an intercept-only linear model, or a slope-containing linear model. If the linear model with slope fit the

proportion data across time better than the intercept only model, this would indicate a systematic increase or decrease in the effect of SR across time.

Hypothesis 3: Recording duration-dependent behavior was explored by investigating the stability of the proportion of best-fit models over increasing recording durations. To investigate this, each participant's 300-second nGVS amplitude trial (0 μ A, 100 μ A, 200 μ A, 300 μ A, 500 μ A, and 700 μ A, for both no foam and with foam) was divided into ten segments of different lengths (30 seconds, 60 seconds, 90 seconds, and so on to 300 seconds). The variable segment lengths were extracted using a random start position within the 300-second trials. The methods from hypothesis 1 were then repeated for each outcome measure (COP area and COP path length) and condition (no foam and with foam) using the variable length data with the intent to determine if the length of data collection effects how often the SR model is the best fit. Similar to hypothesis 2, the proportion of participants whose data was best fit by the SR model in each duration length were fit with two linear models, an intercept-only and a slope-containing model, to determine which model fit the data best. If the linear model with slope fit best, it would indicate that the SR phenomenon is dependent on recording duration.

Hypothesis 4: In order to determine whether SR-like behavior is more prominent when standing on a compliant, unstable surface compared to a stable surface, the proportion of times the SR model was the best fit in each condition (with foam/no foam), across participants, for each COP measure, as determined in hypothesis 1, were compared using a two-proportion Z-test.

Hypothesis 5: In order to investigate whether an intermediate range of stimulation amplitudes produced the highest proportion of “lowest” outcome measures (smallest COP area and shortest COP path length), the number of times each amplitude produced the “lowest” outcome measure was tabulated across all participants.

Aim 2: To determine how frequently an SR-like pattern could arise in measures of postural sway simply by chance, the 300-second sham recordings (0 μ A, with foam and no foam) for each individual participant were divided into six, 30-second segments (the normal recording duration in prior studies). These 30-second segments were then fit with the SR and linear models and compared using the methods described in hypothesis 1, to determine which model fit the data more frequently.

RESULTS

General Results

All of the participants were able to maintain standing balance throughout all of the 12 trials and the control, however, most participants found it more difficult than expected to stand on the foam with their feet together and their eyes closed. Five of the participants commented that they could feel a sensation behind their ears during the highest amplitude trials (700 μ A) which is to be expected as this is where nGVS begins to be perceivable. Two participants commented that they perceived worse balance when they completed the 700 μ A trial and two different participants mentioned that they felt improved balance on the 200 μ A trial and the sham (0 μ A) trial. Participants were never informed of whether the amplitude intensities were being altered nor of what nGVS

amplitude was being delivered. None of the participants experienced any adverse effects to the stimulation. All the participants reported feeling relaxed or lethargic at the end of the testing period.

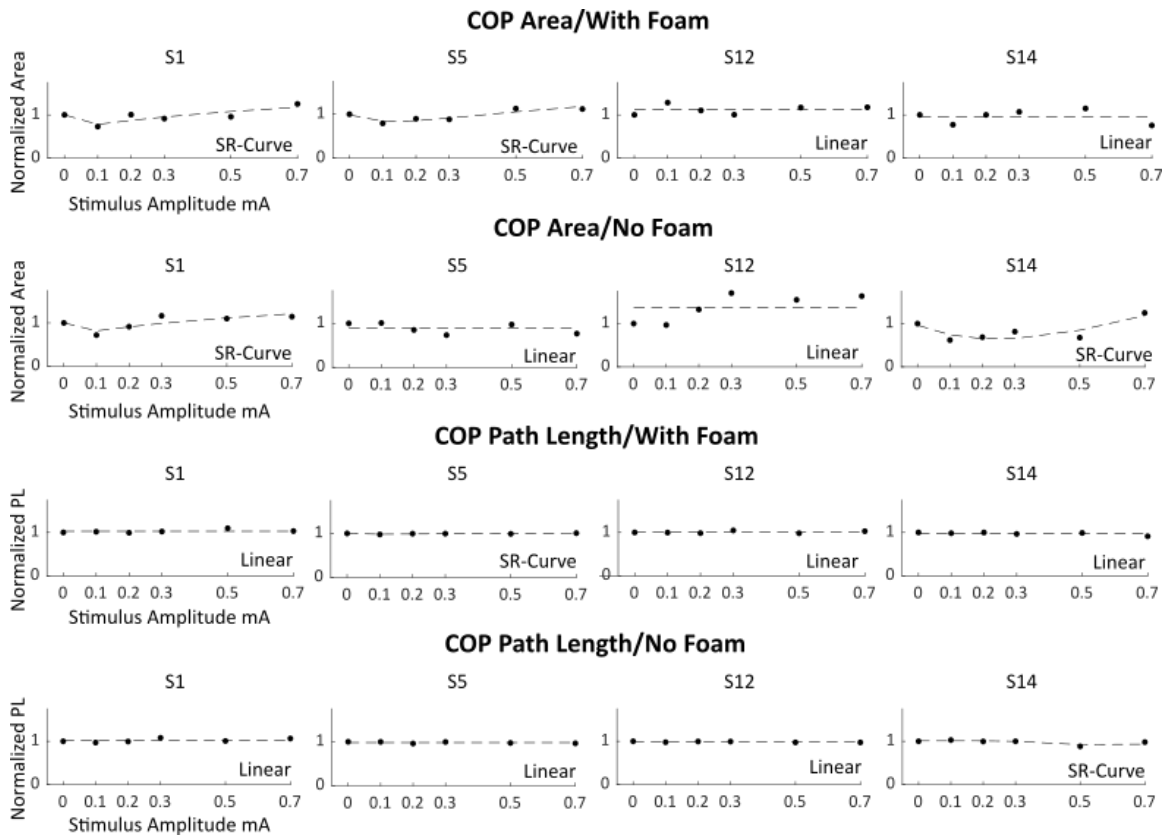
Specific Aims Results

Hypothesis 1: Using 300-second recording trials, only 6 -25% of the data fit the SR model better than the linear model for both COP area and COP path length and each condition (no foam/with foam). More specifically, four of 16 participants demonstrated SR-like behavior in the COP area/no foam measure with the decrease in COP area being $25.3 \pm 11.5\%$ ($M \pm SD$). Four of 16 participants demonstrated SR-like behavior in the COP area/with foam measure with a decrease from baseline of $22.4 \pm 3.6\%$ ($M \pm SD$). Two of 16 participants demonstrated SR-like behavior in the COP path length/no foam measure with a decrease from baseline of $7.9 \pm 5.4\%$ ($M \pm SD$) and only one of 16 participants demonstrated SR-like behavior in the COP path length/with foam measure with a percent decrease of 1.8%. (For examples of how the SR and the linear model fit individual participant data see Figure 7).

Hypothesis 2: When the 300-second recording period was broken into ten 30-second consecutive segments, the highest proportion of the SR model as the best fit, across all of the participants, was found in the COP area/with foam measure at the sixth 30-second segment (150-180 seconds), with approximately 56% of the group having the SR model be the best fit. The majority of the higher proportions of SR models as the best fit were found in the COP area measure, however, none of the 30-second segments had

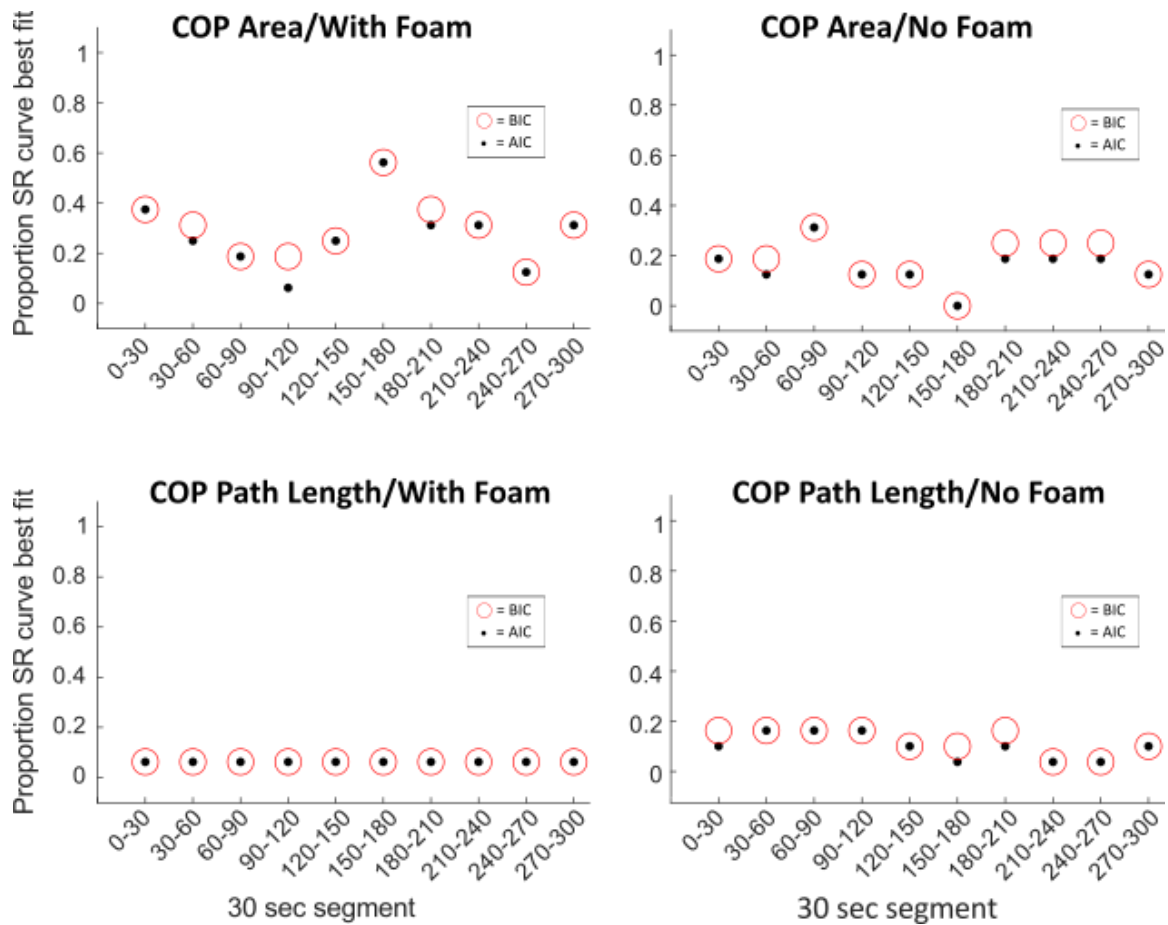
Figure 7

Individual Participant Data Fit with the SR and Linear Models



Note. Each pane represents an individual participant's data fitted with the best-fit model (SR or linear). Black dots represent individual participant data at that nGVs amplitude and the segmented line is the best-fit model. Each measure's data was normalized by dividing the result by the data from the sham condition (the first data point). Normalized Area = Normalized COP area, Normalized PL = Normalized COP path length.

the SR model as the best fit more than 60% of the time in either foam condition (Figure 8). The proportion of times the SR model was the best fit in the COP area/with foam varied between 10% and 56% across all the 30-second segments. The proportion of times the SR model was the best fit in the COP area/no foam measure varied between 5% and 40% across all of the 30-second segments (Figure 8).

Figure 8*Time-Dependent Analysis of 30-Second Segments*

Note. Analysis of 30-second segments reveal that the proportion of times the SR model was the best fit, across participants, was below 40% ($0.4 * 100$) in all but one 30-second segment in the COP area/with foam data. The percent of times the SR model was the best fit, across participants, was less than 10% across the 30-second segments in the COP path length/with foam data and less than 40% for the COP path length/no foam data. The red circle indicates the BIC determination that the SR model was the best fit and the black dot indicates the AIC determination that the SR model was the best fit.

In contrast, the proportion of times the SR model was the best fit in the COP path length/with foam was less than 15% across all the 30-second segments. The COP path length/no foam measure varied between 6% and 19% across all of the 30-second

segments (Figure 8). The linear analysis of the proportion of SR models as the best fit across time found that in all cases, adding a slope parameter did not improve the model fit above an intercept only model, indicating that there was no increase or decrease in the proportion of SR fit over time (Table 1).

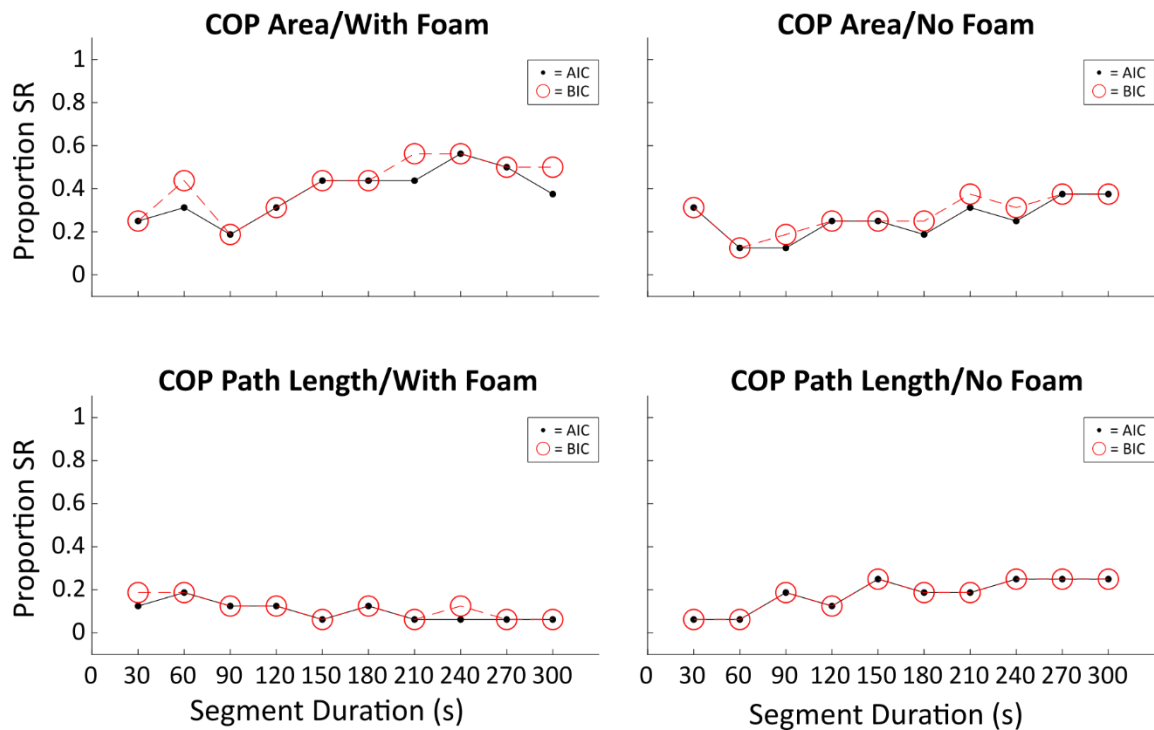
Table 1

Statistical Trend Over Time Analysis of 30-Second Segments

AIC	df	F-Statistic	p-Value
COP Area/Foam	8	0.205	0.662
COP Area/No Foam	8	0.208	0.661
Path Length/Foam	8	0.859	0.381
Path Length/No Foam	8	3.77	0.0882
BIC			
COP Area/Foam	8	0.0536	0.823
COP Area/No Foam	8	0.0116	0.917
Path Length/Foam	8	0.859	0.381
Path Length/No Foam	8	4.49	0.0669

Note. Analysis of the trend over time using 30-second segments revealed no increasing or decreasing trend in either measure (COP area or COP path length) or condition (with foam or no foam) with either information criteria method (AIC or BIC). The f-statistic is for the comparison between the linear model including a slope parameter and the intercept-only model (no slope).

Hypothesis 3: To determine if data-collection duration influenced how often the SR model is the best fit to the data, each model was fit to data segments of different lengths. The different segment durations (30 seconds, 60 seconds, 90 seconds, 120 seconds) were quite variable in terms of the proportion of times the SR model was the best fit. The percentage of SR as the best fit varied from 6% to 56%, with this range depending on which length data segments were used (Figure 9).

Figure 9*Duration-Dependent Analysis of Different Length Segments*

Note. The proportion of SR models as the best fit to the varying segment durations of data are below 60% for both the COP area and COP path length (no foam and with foam). The red circle indicates the BIC determination that the SR model was the best fit and the black dot indicates the AIC determination that the SR model was the best fit.

The means and standard deviations of the proportion of the SR model as the best fit for each measure and condition can be found in Table 2. In looking into whether there was a duration-dependent effect the linear analysis of the proportion of SR models as the best fit across duration found that adding a slope parameter improved the model fit above an intercept only model in some cases. For these particular segments there was an increasing trend in the proportion of times the SR model was the best fit with increasing recording duration (see Table 3).

Table 2

Means and Standard Deviations of the SR Model as Best Fit to Different Segment Lengths of Data-Collection Durations

Segment Duration	Mean	SD
AIC		
COP Area/with foam	0.38	0.12
COP Area/no foam	0.26	0.09
Path Length/with foam	0.10	0.04
Path Length/no foam	0.18	0.08
BIC		
COP Area/with foam	0.42	0.05
COP Area/no foam	0.28	0.09
Path Length/with foam	0.11	0.05
Path Length/no foam	0.18	0.09

Note. Means and standard deviations (SD) of the proportion of the SR model as best fit to varying lengths of recording durations.

Importantly, one limitation of this current analysis is that whether the sloped line significantly improves upon the intercept only line largely depends on the random start point of the segments drawn. If different segments are drawn sometimes no significant trends are observed.

Hypothesis 4: Changing the compliance of the surface (no foam versus with foam) did not increase the proportion of times the SR model was the best fit using either COP area ($Z = 0$) or COP path length ($Z = -0.7559$). Of note, the linear model was also more than twice as likely than the SR model to be the better fit in the COP area and COP path length measures on the firm surface as well as the compliant surface (Figure 10).

Table 3*Statistical Trend Over Data-Collection Duration Analysis of Different Length Segments*

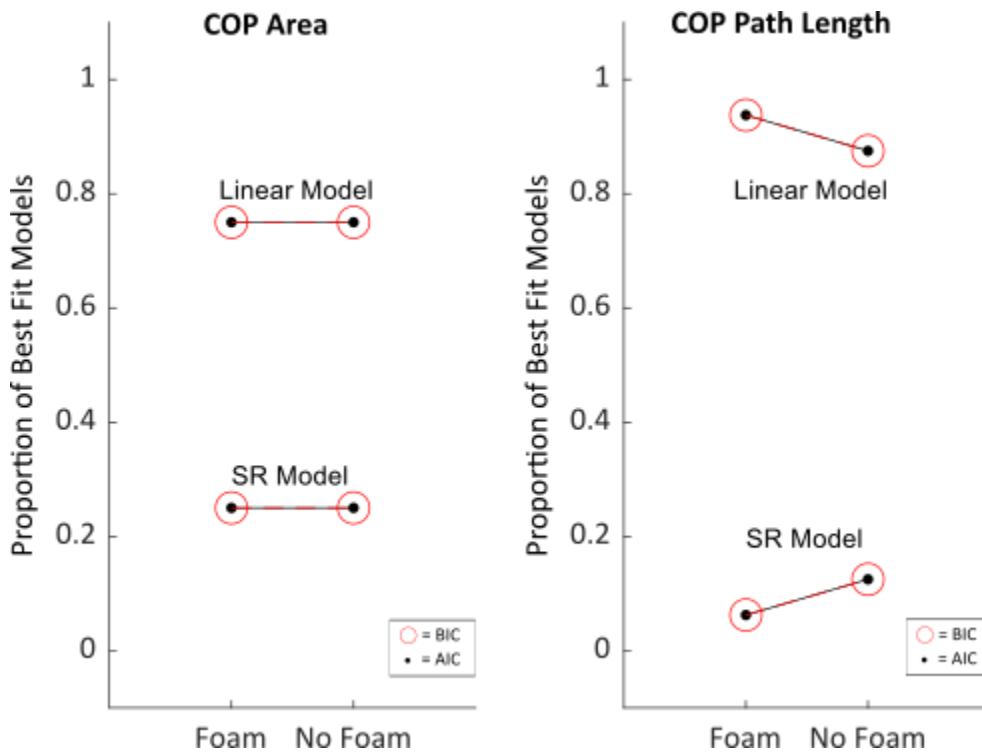
AIC	df	F-Statistic	p-Value
COP Area/Foam	8	9.84	0.014
COP Area/No Foam	8	5.01	0.056
Path Length/Foam	8	13	0.007
Path Length/No Foam	8	19.6	0.002
BIC			
COP Area/Foam	8	10.8	0.011
COP Area/No Foam	8	8.53	0.019
Path Length/Foam	8	13.4	0.006
Path Length/No Foam	8	19.6	0.002

Note. Analysis of the trend over duration using increasing recording durations revealed no increasing or decreasing trend in either measure (COP area or COP path length) or condition (no foam or with foam) with either information criteria method (AIC or BIC). The f-statistic is for the comparison between the linear model including a slope parameter and the intercept-only model (no slope).

Hypothesis 5: As a last attempt to identify the presence of SR in the data, the stimulation amplitudes that produced the lowest outcome measures were tabulated across participants, for both COP area and COP path length. The lowest COP areas were most frequently found at 100 μ A followed by 0 μ A and 300 μ A, and the lowest COP path length results were observed during the sham trial at 0 μ A. Additionally, the lowest COP area results were least likely to be found at 700 μ A whereas the lowest COP path length results were least likely to be found at 500 μ A (Figure 11).

Figure 10

Comparisons of Trials Performed on Firm and Compliant Surfaces

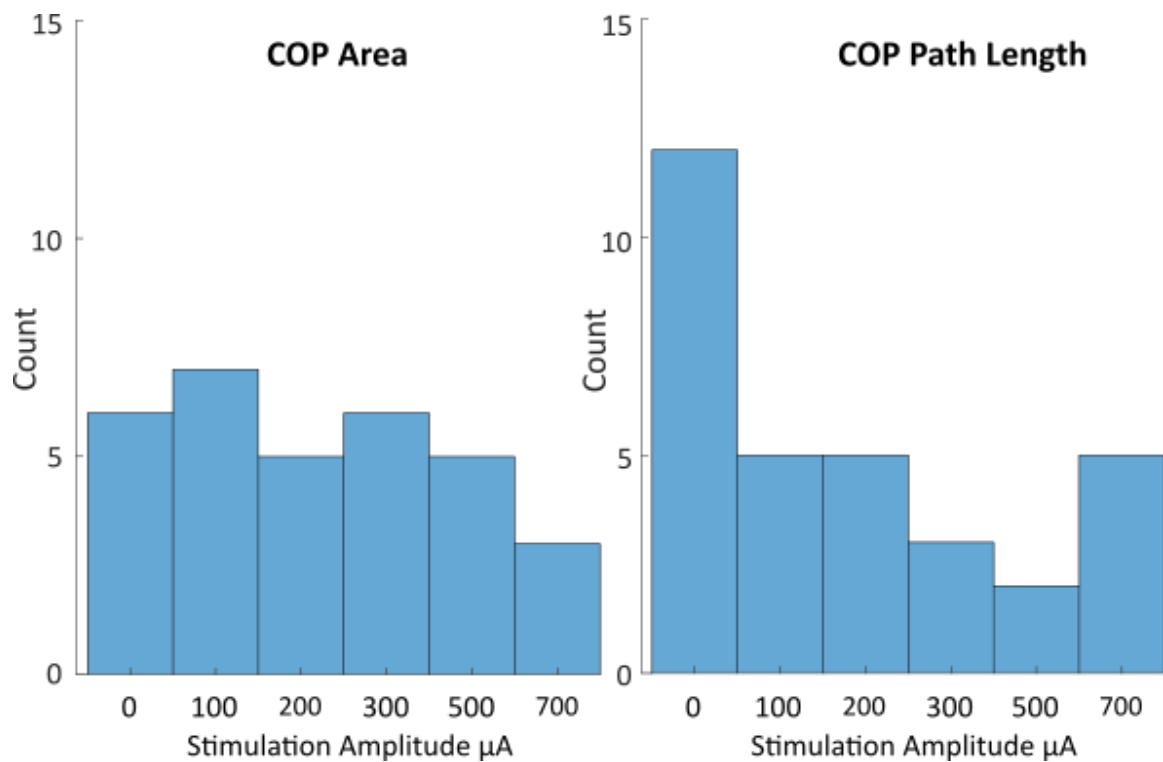


Note. Analysis of the comparisons between the fit of the SR and the linear model to data collected during the no foam and with foam conditions. The red circle indicates the BIC determination that the SR model was the best fit and the black dot indicates the AIC determination that the SR model was the best fit.

Aim 2: To determine how frequently an SR-like pattern would arise in measures of postural sway simply by chance, the SR model best fit the COP area data from the 0 μ A trials as much as 44% of the time in the foam/sham condition, as much as 25% of the time in the no foam/sham condition, and 25% of the time in the control (Figure 12). In the COP path length data, the SR model best fit the data 0 μ A data approximately 38% of the time in the foam/sham condition, approximately 25% of the time in the no foam/sham condition, and 50% of the time in the control (Figure 12). Of the sham trials

Figure 11

Incidences of Lowest COP Measures Across Amplitude Intensities

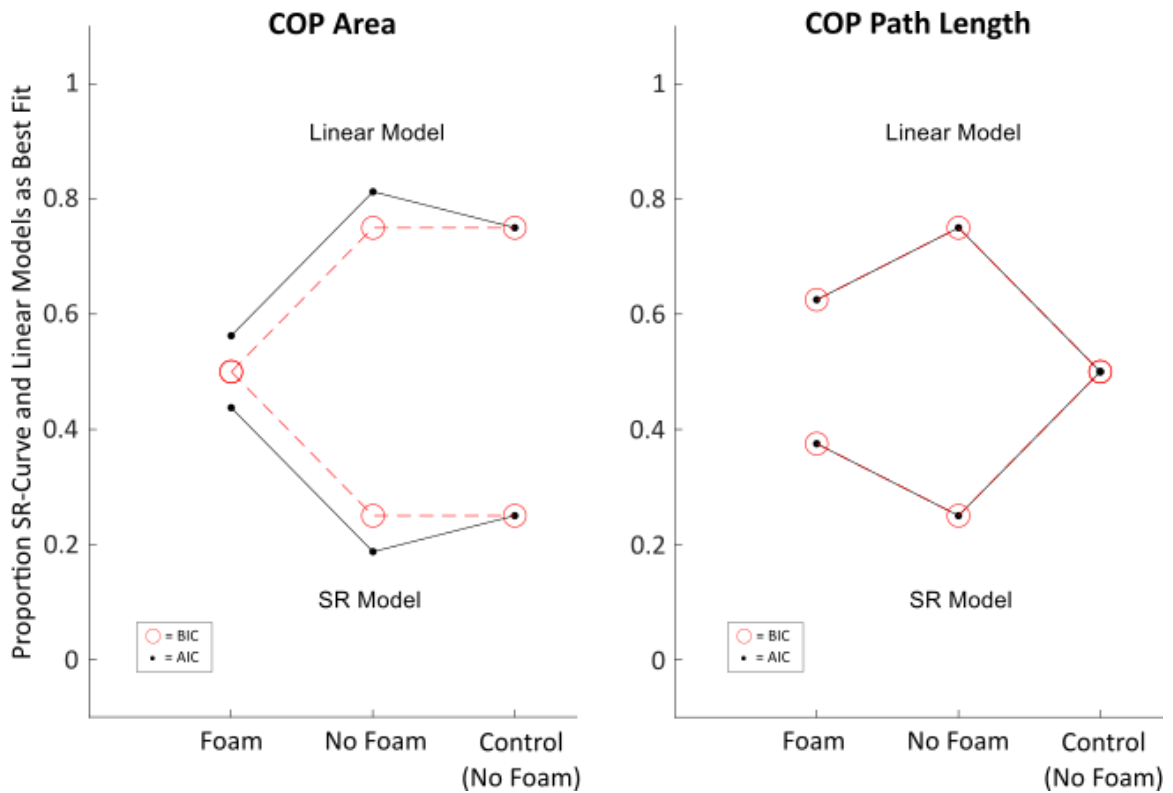


Note. Incidences of lowest COP area and lowest COP path length results at each stimulation amplitude across all participants. If SR is present each histogram should follow an inverted U like pattern.

that fit the SR model, the mean percent decrease in the COP area/with foam from baseline was $19.1 \pm 19.6\%$ ($M \pm SD$). The mean percent decrease in the COP area/no foam from baseline was $39.3 \pm 24.0\%$ ($M \pm SD$). The mean percent decrease in the COP path length/with foam from baseline was $1.9 \pm 1.5\%$ ($M \pm SD$). The mean decrease in the COP path length/no foam measure was $1.5 \pm 1.8\%$ ($M \pm SD$).

Figure 12

Likelihood of Observing SR-Like Behavior by Chance



Note. Proportion of SR and linear models as best fit to 0 μ A stimulation trials for each individual participant, demonstrating the likelihood that SR-behavior can arise by chance. The red circle (and segmented line) indicates the BIC determination that the SR model was the best fit and the black dot (and solid line) indicates the AIC determination that the SR model was the best fit. The top three circles in both panels are the proportion of times the linear model was the best fit and the bottom three circles the proportion of times the SR model was the best fit.

DISCUSSION

In this study I set out to determine whether postural stability is affected by the application of nGVS in a manner consistent with the presence of SR, by using a longer than typical recording duration of 300-seconds. In order to reveal SR, 16 healthy

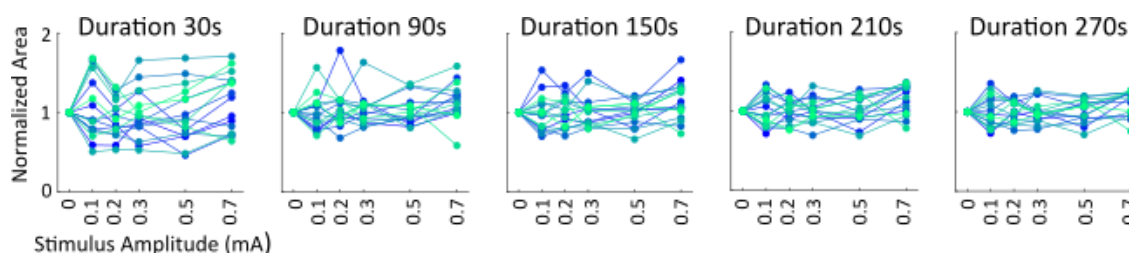
young participants were provided with nGVS amplitude intensities ranging from 0 μ A to 700 μ A. The raw force plate data was used to calculate COP area and COP path length for each participant under two conditions (no foam and with foam) which were fit with an SR and a linear model. Then, the two models were compared using AIC and BIC, in order to determine which model fit the data best. Assuming SR as the driving force behind the behavioral response to nGVS, changes in each COP measure should follow pseudo-bell-shaped SR-curve, indicating a minimum at an intermediate stimulation amplitude (see Figure 2). In this study, decreases in COP area and COP path length were observed at some nGVS amplitudes in a subset of participants, however, the decreases were randomly scattered across stimulus amplitudes within participants, which is not consistent with an SR-enhanced performance (the *SR curve*). In agreement with a recent paper by Asslander et al. (2021), there were no obvious signs of SR behavior and the times the SR model produced the best fit were not beyond what would be observed as a result of chance. Therefore, these results suggest that if SR is present in healthy young adults its effect may be too small to distinguish from random noise.

The intent behind using the longer sampling duration in this study was to allow for less variability in the data and therefore provide better estimates of participants' behavior across stimulation amplitudes and thus better insights into SR as the underlying mechanism. As expected, the increase in recording duration did indeed decrease the variability of the COP area and COP path length measures (Figure 13). However, duration's effect on SR model fit was less clear. In the fit presented here (Figure 9), there was a trend of increasing frequency of SR-fit with duration, as might be

expected if SR is present, and supporting the use of a longer 300 second recording duration. However, because the frequency of SR-fit with different data lengths was highly variable, due to its dependency on the specific data segment analyzed, caution must be taken in what is inferred about this relationship from these data. Consideration of such variability is important, however, because many nGVS studies tend to collect data for relatively short durations (30-60 seconds), which may have contributed to the variability in their reported results. Previously, van der Kooij and colleagues (2011) criticized the field of static posturography for its lack of standardization pertaining to recording durations. In particular, van der Kooij et al. (2011), stressed that COP measures are significantly influenced by recording durations and that short recording durations can lead to conflicting results between studies. The authors also found that recording durations of at least 300 to 360 seconds are required in order to attain reliable measures from COP when the eyes are closed.

Figure 13

Variability of Proportion of SR model as Best Fit Over Increasing Sampling Durations



Note. The variability of the COP area measure decreases and stabilizes as sampling duration increases.

In further support of the conclusion that SR-like effects are small or are not present in healthy young adults, I found no evidence of an increase in the frequency of

the SR model being the best fit with increased instability. Indeed, there was no statistical difference between the foam and no foam conditions in either COP measures indicating that the stability of the surface has little impact on the frequency of observing SR-like behavior. In fact, a trend to the opposite of what would be expected was found in the COP path length measure as the SR model fit the data in the no foam condition more frequently than in the foam condition (hypothesis 4), though not statistically so. Moreover, tabulation of the stimulation amplitude that produced the “lowest” COP measure yielded a result that was also not what would be expected if SR were present. If SR were present, the histogram should have exhibited an inverted U like behavior with the middle bins of the histograms being higher than the 0 μA and 700 μA bins, indicating that the participants experienced reductions in COP measures most often during delivery of the mid-range stimulation amplitudes (100 μA , 200 μA , 300 μA , 500 μA). Instead, the opposite occurred in the COP path length measure, where the smallest COP measure was observed most frequently in the 0 μA stimulation condition.

As previously mentioned, this study found that the SR model only fit the data best during the nGVS stimulation trials 6% to 25% of the time. This was less than what was observed by chance using 30-second segments of the sham (0 μA) trials (see aim 2). In the stimulation trials, the SR model fit the COP area/no foam measure 25% of the time, COP area/with foam measure 25% of the time, COP path length/no foam measure 12.5% of the time and COP path length/with foam measure 6.25% of the time. Meanwhile, in the sham trials, the SR model fit the COP area/no foam measure 25% of the time, COP area/with foam measure 44% of the time, COP path length/no foam

measure 25% of the time and COP path length/with foam measure 38% of the time. In short, the SR model fit the data more often during the sham trials than the stimulation trials, suggesting, that the SR model fits during stimulation trials were likely indistinguishable from chance events in these young healthy participants, at least based on the SR identification criteria defined here. Interestingly, the decrease in COP measures during stimulation and sham trials were similar. The mean decrease of the COP area from baseline was 22.4% in the with foam stimulation trials versus 19.1% in the with foam sham trials, and 25.3% in the no foam stimulation versus 39.3% in the no foam sham trials. The mean percent decrease in the COP path length from baseline was 1.7% in the with foam stimulation trials versus 1.9% in the with foam sham trials, and 7.9% in the no foam stimulation trials versus 1.5% in the no foam sham trials. Previous studies have found similar decreases of 5 to 40% in postural sway measures during nGVS (Inukai, Otsuru, et al., 2018; Iwasaki et al., 2014; Mulavara et al., 2011).

Alternative Mechanisms

The hypothesis that SR is the mechanism driving the response to low amplitude nGVS is found in much of the research in this field. However, this explanation may not tell the whole story (Fujimoto et al., 2016; Fujimoto et al., 2018; Mulavara et al., 2011; Mulavara et al., 2015; Piccolo et al., 2020; Samoudi et al., 2015; Sprenger et al., 2020; Temple et al., 2018; Woll et al., 2019; Wuehr, Nusser, Decker, et al., 2016; Wuehr, Nusser, Krafczyk, et al., 2016). Indeed, other mechanisms have been proposed to be working in combination with SR or as alternatives to the SR phenomenon (Goel et al., 2015; Inukai, Masaki, et al., 2018; Inukai, Otsuru, et al., 2018; Iwasaki et al., 2018). In a

series of studies investigating the effect of sub-sensory vestibular stimulation applied in the mediolateral direction during cross-planar balance, Goel et al., (2015) proposed that the added noise may affect the CNS in addition to enhancing signal detection at the vestibular afferent and end organ level. Similarly, Inukai, Masaki, et al. and Inukai, Otsuru, et al. (2018) hypothesized that the postural responses observed in their studies could have been induced by the activation of multisensory cortical areas as well as the brain regions involved in vestibular information processing, such as the supramarginal gyrus, posterolateral thalamus, cerebellar vermis, posterior insula and hippocampus. Such increased cortical activation does not seem congruent with a simple increase in encoding efficacy but perhaps instead a change in baseline vestibular noise or activity. Also, in their study of the effects of nGVS on locomotion, Iwasaki and colleagues (2018) suggested that nGVS may interact with the cerebellum as this part of the brain is involved in coordinating gait speed and gait pattern, which could explain the increase in stride length and gait velocity seen in their study. Lastly, Fujimoto et al., (2016) suggest neuroplasticity in the vestibular nucleus and cerebellum could explain the sustained improvements in postural stability they observed after 30 minutes of nGVS. Similarly implying something more than a simple improvement in encoding efficacy.

Regardless of the mechanism, it is peculiar that such effects are not (easily) observed in healthy young adults. Presumably, this population should also be impacted by this mechanism. Given the effect of nGVS on other vestibular derived measures, an absence of effect in this population would suggest a posture specific filter. But this raises new questions regarding how the body might separate nGVS derived signal from

natural vestibular signals. Perhaps the simplest explanation is that the effect is present in young adults but is simply too small to be easily extracted using highly variable sway measures.

Future Research

Interestingly, a common observation among nGVS balance studies is that participants with vestibular impairments and/or less balance control at baseline tend to show more effect of the nGVS than participants with normal balance at baseline (Fujimoto et al., 2019; Herssens & McCrum, 2019; Inukai, Otsuru, et al., 2018; Inukai, Masaki, et al., 2018). Given that our results are limited by the use of young healthy participants, who presumably have healthy vestibular processing and therefore may not benefit as much from the addition of external noise, future SR research should focus on elderly participants as well as participants with vestibular impairments. Considering the greater response to nGVS observed in these populations, they may be essential to determination, or validation, of the mechanism underlying these SR-like behavioral changes.

Another approach to exploring the mechanism behind nGVS would be to look at non-responders. Many studies find that a portion of their participants do not respond to nGVS at all or do not have an optimal response to nGVS (Goel et al., 2015; Fujimoto et al., 2016; Iwasaki et al., 2014). This “non-responder” group could provide some interesting insight into the mechanism driving the nGVS response. Goel et al., (2015) speculated that non-responders are individuals who utilize visual and proprioceptive cues more than vestibular sensory information to maintain postural stability and therefore remain un-affected by vestibular stimulation. However, healthy individuals

usually rely on all three sensory systems (visual, somatosensory, and vestibular) to varying degrees to navigate their environment and maintain balance. The degree to which one sensory system “takes the lead” over the other two is constantly being adjusted depending on the situation (Horak, 2016). Therefore, healthy non-responders could be recruited and tested in a visual and proprioception-controlled environment to pinpoint why nGVS does not affect them and as a consequence determine why it affects others.

Finally, the nGVS procedures need to be improved in order to gain common grounds on which to compare nGVS studies to one another. The use of different frequency bandwidths, stimulation intensities, thresholding tasks, performance tasks and postural conditions has made interpretation and comparison between results more challenging.

CONCLUSION

This study did not find evidence of SR-like behavior in healthy young adults but did provide evidence of greater variability found in shorter recording durations that could lead to more frequent observation of spurious SR-like behavior due to random chance. Therefore, longer recording durations could provide future nGVS balance studies more reliable results. Noisy GVS research is important because of its potential to lead to the development of prostheses to help prevent falls in populations with vestibular impairments. However, improvements to the methods used in this research are necessary in order to more quickly advance toward the realm of clinical intervention.

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